K080910

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS FEB - 4 2009

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR §807.92(c)

Submitted by:
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Date summary prepared: March 31, 2008
Date summary updated: October 2, 2008

Trade Name: PATHIAM™ System with iScan for HER2/neu

Classification Name: Microscope, Automated Image Analysis, Operator Intervention (NOT), primary and Automated Digital Image Manual Interpretation, Microscope (OEO) secondary.

Device Description:
The PATHIAM™ System is an instrument (iScan) and image analysis software system designed to assist the qualified pathologist in the consistent quantitative assessment of marker expression in immunohistochemically stained histological sections digital images. The sample tissue is breast tissue prepared using the DAKO HercepTest Reagent Kit. The PATHIAM system consists of the BioImagene iScan slide scanner, computer with the PATHIAM Software, monitor, keyboard and mouse.

The PATHIAM System digitizes formalin-fixed, paraffin embedded normal and neoplastic tissue and provides semi-quantitative analysis of extent and intensity of stained tissue, providing the pathologist with an aid to interpretation of the level of expression of HER2/neu in breast cancer tissue. The pathologist is presented with a digital image of the tissue section and a suggested staining score (0 to 3). The pathologist then makes an

assessment of the digital image and reports his/her score. Alternately, the pathologist can simply use the digitized image to perform his interpretation of the level of expression, without employing the software.

Hardware: The iScan slide scanning device captures digital images of formalin-fixed, paraffin-embedded tissues that are suitable for storage, viewing and visual analysis. The device includes a digital slide scanner, racks for loading glass slides, an Intel based PC, dual core, dual Xeon processor, PATHIAM Software, and a monitor.

Software: The PATHIAM Software requires competent human intervention at all steps in the analysis process. The system is designed to complement the routine workflow of a qualified pathologist screening the immunohistochemically stained histological slides with additional quantitative data to assist the reproducibility of the slide interpretation. It allows the user to select the area of interest on the breast tissue image. The user marks the area of interest for the analysis. The system software makes no independent interpretations of the data. The software will act as a tool for the user, to improve consistency and data recording. The image produced digitally may also be used independent of the software, by allowing the pathologist to count from the digital image, rather than from the microscope.

Indications for Use:
When used with the DAKO HercepTest, it is indicated for use as aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered. The pathologist should verify agreement with the PATHIAM score.

Predicate Device:
PATHIAM Imaging Software for HER2/neu, K062756
Regulation: 21 CFR §864.1860
Product Code: NOT
Panel: Pathology

Performance:

a. Reproducibility Study between Pathologists and PATHIAM Systems
The PATHIAM System was tested by analyzing images of the same set of 176 stained tissue specimens by three pathologists at three sites. Pathologists recorded their estimation of the score from the score provided by the PATHIAM System plus their review of the digital images provided by the software. Concordance for the PATHIAM System values between labs ranged from 89% to 92%.

b. Comparison with Manual HercepTest method
Values for staining intensity were obtained from a review of PATHIAM values by trained pathologists at three sites, who viewed both the digital images and the score provided by the software, and then selected an appropriate tissue score (0 to 3). The same pathologists read the same slides manually using the DAKO HercepTest package insert. The manual assessments took place 7 days before the experiments with the PATHIAM System were completed at the site.

Tables 1-3 – Concordance Between the PATHIAM System and Manual Scores of HercepTest® stained Breast Tissue,

Table 1. Site 1. Manual vs PATHIAM

Site 1	Manual 0-1+	Manual 2+	Manual 3+
PATHIAM 0-1+	71	17	4
PATHIAM 2+	0	25	19
PATHIAM 3+	0	1	39

Percent Agreement =135/176 X 100 = 77%
Overall % agreement (95% EXACT CI): 77% (70% - 83%)

Table 2. Site 2. Manual vs PATHIAM

Site 2	Manual 0-1+	Manual 2+	Manual 3+
PATHIAM 0-1+	80	4	0
PATHIAM 2+	13	37	0
PATHIAM 3+	0	16	26

Percent Agreement =143/176 X 100 = 81%
Overall % agreement (95% EXACT CI): 81% (75% - 87%)

Table 3. Site 3. Manual vs PATHIAM

Site 3	Manual 0-1+	Manual 2+	Manual 3+
PATHIAM 0-1+	86	7	0
PATHIAM 2+	3	28	9
PATHIAM 3+	0	2	41

Percent Agreement =155/176 X 100 = 88%
Overall % agreement (95% EXACT CI): 88% (82% - 92%)

Tables 4-6 – Comparison Manual Scoring between Sites

Table 4. Site 1 vs 2. Manual vs Manual

Site 1 vs. 2	Manual 0-1+	Manual 2+	Manual 3+
Manual 0-1+	70	1	0
Manual 2+	21	22	0
Manual 3+	2	34	26

Percent Agreement = 118/176 X 100 = 67%
Overall % agreement (95% EXACT CI): 67% (60% - 74%)

Table 5. Site 2 vs 3. Manual vs Manual

Site 2 vs. 3	Manual 0-1+	Manual 2+	Manual 3+
Manual 0-1+	86	7	0
Manual 2+	3	30	24
Manual 3+	0	0	26

Percent Agreement = 142/176 X 100 = 81%
Overall % agreement (95% EXACT CI): 81% (74% - 86%)

Table 6. Site 3 vs 1. Manual vs Manual

Site 3 vs. 1	Manual 0-1+	Manual 2+	Manual 3+
Manual 0-1+	69	20	0
Manual 2+	2	22	13
Manual 3+	0	1	49

Percent Agreement =140 /176 X 100 = 80%
Overall % agreement (95% EXACT CI): 80% (73% - 85%)

Tables 7-9 – Comparison PATHIAM Scoring between Sites

Table 7. Site 1 vs 2. PATHIAM vs PATHIAM

Site 1 vs. 2	PATHIAM 0-1+	PATHIAM 2+	PATHIAM 3+
PATHIAM 0-1+	83	9	0
PATHIAM 2+	1	40	3
PATHIAM 3+	0	1	39

Percent Agreement =162/176 X 100 = 92%
Overall % agreement (95% EXACT CI): 92% (87% - 96%)

Table 8. Site 2 vs 3. PATHIAM vs PATHIAM

Site 2 vs. 3	PATHIAM 0-1+	PATHIAM 2+	PATHIAM 3+
PATHIAM 0-1+	82	2	0
PATHIAM 2+	11	35	4
PATHIAM 3+	0	3	39

Percent Agreement =156/176 X 100 = 89%
Overall % agreement (95% EXACT CI): 89% (83% - 93%)

Table 9. Site 3 vs 1. PATHIAM vs PATHIAM

Site 3 vs. 1	PATHIAM 0-1+	PATHIAM 2+	PATHIAM 3+
PATHIAM 0-1+	88	5	0
PATHIAM 2+	4	34	2
PATHIAM 3+	0	5	38

Percent Agreement =160/176 X 100 = 91%
Overall % agreement (95% EXACT CI): 91% (86% - 95%)

c. BioImagene iScan Slide Scanner Reproducibility

1. iScan Slide Scanner Precision

   Eight samples, two each with manual scores of 0, 1+, 2+ and 3+ were scanned 5 times on the iScan slide scanner. The precision was calculated to be 97%.

2. Inter-run/Inter System Reproducibility

   Eight samples, two each with manual scores of 0, 1+, 2+ and 3+ were scanned 5 times on 3 different iScan slide scanners. The agreement between the PATHIAM System scores for different scans is 100% and for different iScan slide scanners was 100%.

d. Substantial Equivalence

Table 13: Comparison to Predicate Devices to Support Substantial Equivalence Determination

Attribute	**PATHIAM Software (predicate)**	**PATHIAM System**
Intended Use	The imaging software is intended to detect and classify cells of clinical interest by analyzing digitized images of microscope slides based on object identification of cellular objects of particular intensity, shape, size and color. The software can be used with a computer and image digitizer with features specified in the labeling.	The PATHIAM System consists of the PATHIAM Software, the BioImagene iScan Slide Scanner, computer, keyboard, monitor and mouse intended to detect and classify cells of clinical interest by analyzing digitized images of microscope slides based on object identification of cellular objects of particular intensity, shape, size and color.
Indications for use	When used with the DAKO HercepTest, it is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN®	Same

Attribute	PATHIAM Software (predicate)	PATHIAM System
	(Trastuzumab) treatment is being considered. The pathologist should verify agreement with the PATHIAM score.	
Specimen Type	Formalin-fixed, paraffin embedded specimens stained by immunohistochemistry reagent for HER2/neu	Same
Image Analysis System	Histologic observation by a pathologist through a specified microscope/digital camera combination or slide scanner.	Histologic observation by a pathologist through the BioImagene iScan slide scanner.
Method of Cell Detection	Object identification of a digitized field of view of a pathology slide, using size, shape, color and intensity as observed by a software, and by visual observation of the digitized image by a health care professional.	Same
Hardware Components	Computer, either microscope with digitizing camera or slide scanner, keyboard, mouse, high resolution color monitor, and hard drive for storage.	PATHIAM Software, BioImagene iScan slide scanner, computer, and monitor.
Assay used	DAKO HercepTest™	Same

Standards Employed

None under Section 514

FDA Guidance

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, May 11, 2005

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB - 4 2009

BioImagene, Inc.
c/o Mr. Indu Lakshman
Director of QA & RA
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Re: k080910
Trade/Device Name: PATHIAM System with iScan for HER2/neu
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry Reagents and Kits
Regulatory Class: Class II
Product Code: NOT
Dated: January 16, 2009
Received: January 21, 2009

Dear Mr. Lakshman:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (240) 276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at (240) 276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Maria M. Chan, Ph.D.
Acting Division Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation
and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K080910

Device Name: PATHIAM System with iScan for HER2/neu

Indication For Use:

PATHIAM-Assisted Scoring: Intended for clinical laboratory use as an accessory to the DAKO HercepTest to aid in the detection and semi-quantitative measurement of Her2/neu in formalin fixed, paraffin-embedded normal and neoplastic tissue. When used with the DAKO HercepTest, Pathiam Assisted Scoring is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN (Trastuzumab) treatment is being considered. The pathologist should verify agreement with the PATHIAM System score.

HER2/neu results are indicated for use as an aid in the management, prognosis and predication of therapy outcomes of breast cancer. Note: The actual correlation of the DAKO HercepTest to Herceptin® clinical outcome has not been established.

Prescription Use ___X___ And/Or (21 CFR Part 801 Subpart D)

Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Josephine Gautier

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K080910